REMARKS

The Office Action and the cited and applied references have been carefully reviewed. No claim is allowed. Claims 12, 15-19, 21, and 24-33 presently appear in this application and define patentable subject matter warranting their allowance. Reconsideration and allowance are hereby respectfully solicited.

Claims 24 and 25 have been rejected as being anticipated by Kaltoft et al., US 2002/0001841, with priority to U.S. provisional application 60/091,684, filed July 2, 1998. This rejection is respectfully traversed.

The claim for priority to the July 31, 1998, filing date of the French priority document has been perfected by the filing of a certified English translation of the priority document with the amendment dated July 14, 2004. Accordingly, the June 25, 1999, filing date of US 2002/0001841 (appl. no. 09/339,836) is antedated by applicants' priority date of July 31, 1998. While it is noted that US 2002/0001841 claims the benefit of priority to provisional application 60/091,684, filed July 2, 1998, this provisional application is not available as a §102(e) reference because the paragraph [0150] in Kaltoft cited by the examiner, or a teaching of the caspase inhibitor z-VAD relied upon by the examiner, is not found in 60/091,684. Accordingly,

Kaltoft is not available as prior art under §102(e) and cannot anticipate the presently claimed invention.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Claims 12, 13, 16-19 and 21 have been rejected under 35 U.S.C. §102(e) as being anticipated by Lu, U.S. Patent 6,733,792. This rejection is respectfully traversed.

The claims have been amended to recite a combination of arsenic trioxide and PML protein and/or an agent inducing the overexpression of the PML protein. Lu, however, only discloses combinations of arsenic sulfide and interferons (see column 11, line 65 to column 12, line 16). Moreover, Lu does not disclose the use of a combination of a caspase inhibitor and an interferon. Accordingly, Lu cannot anticipate the presently claimed invention.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

While Lu has not been cited or applied in an obviousness rejection under 35 U.S.C. §103(a), the highly synergistic effect of arsenic trioxide with an interferon in terms of cell death (Example 4, pages 17 to 18) was unexpected and represents an unexpectedly superior result that could not have been obvious to one of skill in the art.

Claims 12-14, 16-19 and 21 have been rejected under 35 U.S.C. §103(a) as being unpatentable over He et al., *Anticancer Research* 17:3927, Abstract#6 (1997) in view of Muller et al., EMBO 17:61-70 (1998) and Chelbi-Alix et al. (1996). This rejection is respectfully traversed.

Even if it would have been *prima facie* obvious to one of ordinary skill in the art to combine arsenic trioxide with interferon for the treatment of leukemias associated with the fusion protein PML/RARalpha, or for the *in vitro* inhibition of leukemia cells, as asserted by the examiner (which applicants do not agree with), the highly synergistic effect shown in Example 4, pages 17-18 of the specification, could not have been predicted. For instance, in the table on page 17, the 60% and 63% positive TUNEL signal obtained for IFNα + zVAD and IFNα + As_2O_3 is substantially higher than an additive effect of IFNα alone (42% of positive TUNEL signal) and either zVAD alone (5% of positive TUNEL signal) or As_2O_3 alone (5.5% of positive TUNEL signal). Accordingly, the unexpectedly superior results obtained by combination of As_2O_3 or zVAD with interferon-α cannot be obvious from He in view of Müller and Chelbi-Alix.

Reconsideration and withdrawal of this rejection are therefore respectfully requested.

Claims 12-19 have been rejected under 35 U.S.C. 112, first paragraph, because the examiner states that the specification, while being enabling for a method inducing cell death comprising the administration of arsenic or arsenic derivative or zVAD or DEVD which promotes the targeting of PML to the nuclear bodies and the administration of an agent which induces the overexpression of the PML protein wherein the death of undesirable cells is not due to apoptosis, does not reasonably provide enablement for a method of stimulating an immune response comprising the administration of a substance which promotes the targeting of PML to the nuclear bodies and the administration of an agent which induces the overexpression of the PML protein, wherein the death of undesirable cells is not due to apoptosis. This rejection is obviated by the amendment to claims 12 and 19 to positively recite that the caspase inhibitor is selected from the group consisting of zVAD and DEVD.

Reconsideration and withdrawal of this rejection are therefore respectfully requested.

New dependent claims 28-33 are added to positively recite a single specific caspase inhibitor and new claims 26 and 27 find support in the specification on page 2, lines 12-22.

In view of the above, the claims comply with 35 U.S.C. §112 and define patentable subject matter warranting their

allowance. Favorable consideration and early allowance are earnestly urged.

Respectfully submitted,

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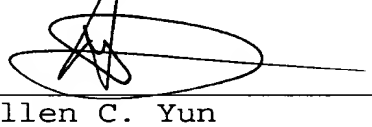
By 
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